

## 9.1 Composition of Parenteral Nutrition: Branched Chain Amino Acids (BCAA)

January 31<sup>st</sup>, 2009

### Recommendation:

*In patients receiving parenteral nutrition, there are insufficient data to make a recommendation regarding the use of branched chain amino acids in critically ill patients.*

**Discussion:** The committee noted the modest treatment effect for mortality with wide confidence intervals. The committee was concerned about the heterogeneity of findings in these 5 studies (test for heterogeneity  $p = 0.16$ ) only one study demonstrating a statistically significant reduction in mortality (Garcia De Lorenzo). Safety was not considered to be a great concern however feasibility and cost were unfavourable.

Values	Definition	Score: 0, 1, 2, 3
Effect size	Magnitude of the absolute risk reduction attributable to the intervention listed--a higher score indicates a larger effect size	2 (mortality)
Confidence interval	95% confidence interval around the point estimate of the absolute risk reduction, or the pooled estimate (if more than one trial)--a higher score indicates a smaller confidence interval	2
Validity	Refers to internal validity of the study (or studies) as measured by the presence of concealed randomization, blinded outcome adjudication, an intention to treat analysis, and an explicit definition of outcomes--a higher score indicates presence of more of these features in the trials appraised	2
Homogeneity or Reproducibility	Similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials	1
Adequacy of control group	Extent to which the control group presented standard of care (large dissimilarities=1, minor dissimilarities=2, usual care=3)	3
Biological Plausibility	Consistent with understanding of mechanistic and previous clinical work (large inconsistencies=1, minimal consistencies=2, very consistent=3)	1
Generalizability	Likelihood of trial findings being replicated in other settings (low likelihood i.e. single centre=1, moderate likelihood i.e. multicentre with limited patient population or practice setting=2, high likelihood i.e. multicentre, heterogenous patients, diverse practice settings=3)	1
Low cost	Estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	1
Feasible	Ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	1
Safety	Estimated probability of avoiding any significant harm that may be associated with the intervention listed--a higher score indicates a lower probability of harm	2

## 9.1 Topic: Composition of Parenteral Nutrition: Branched Chain Amino Acids (BCAA)

January 31<sup>st</sup> 2009

Question: Do BCAA in parenteral nutrition affect outcomes in the critically ill adult patient?

Summary of evidence: There were 5 level 2 studies reviewed.

**Mortality:** There were 4 studies that reported on mortality, 3 of these found no significant difference in mortality between the groups receiving higher amounts of BCAA and lower amounts (von Meyenfeldt 1990, Vanway 1995, Kuhl 1990). Only one study found a significant reduction in mortality ( $p < 0.03$ ) in septic patients receiving 45 % BCAA vs lower (standard) amounts (Garcia de-Lorenzo). Meta-analysis of these studies showed a trend towards a reduction in mortality in the groups receiving BCAA (RR 0.58, 0.26-1.28,  $p = 0.18$ ) (figure 1).

**Infections:** Two studies reported on infections and found no differences in infections with the use of BCAA (Ott 1988 ( $p=0.68$ ), Kuhl 1990).

**LOS and Ventilator days:** Only one study (Garcia de-Lorenzo 1997) reported on LOS but there were no differences between groups.

**Other complications:** Not reported.

### Conclusions:

- 1) Higher levels of BCAA are associated with a trend towards a reduction in mortality, when compared to standard amounts of BCAA.
- 2) No differences found in infections, LOS or ventilated days between groups receiving higher and standard amounts of BCAA.

*Level 1 study: if all of the following are fulfilled: concealed randomization, blinded outcome adjudication and an intention to treat analysis.*

*Level 2 study: If any one of the above characteristics are unfulfilled.*

Table 1. Randomized studies evaluating BCAA (PN) in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)		Infections # (%)‡	
				BCAA	Standard	BCAA	Standard
1) Ott 1988	Brain injured patients N = 20	C.Random: not sure ITT: yes Blinding: no (6)	BCAA (Aminosyn) vs standard PN (travasol)	BCAA NA	Standard NA	BCAA 4/10 (40)	Standard 4/10 (40)
2) Von Meyenfeldt 1990	Septic and traumatized patients N = 101	C.Random: not sure ITT: yes Blinding: double (10)	50 % BCAA vs 16 % BCAA (standard)	BCAA 17/49 (35) hospital	Standard 16/52 ( 31) hospital	BCAA NA	Standard NA
3) Van Way 1995	Mixed surgical population, severely stressed N = 12	C.Random: not sure ITT: yes Blinding: no (7)	45 % BCAA vs 25 % BCAA (standard)	BCAA 1/6 (17) hospital	Standard 4/6 (67) hospital	BCAA NA	Standard NA
4) Garcia De Lorenzo 1997	Septic patients from 7 ICUs N = 69	C.Random: not sure ITT: yes Blinding: no (8)	3 groups: (A) standard BCAA + 1.5 g/kg/day AA (B) 45 % BCAA + 1.5 g/kg/day AA (C) 45 % BCAA + 1.1 g/kg/day AA Compared (B) + (C) TO (A)	(A) 9/22 (41) 10/22 (46)	(B) ICU 2/25 (8) 2/25 (8)	(C) 5/22 (23) 6/22 (27)	NA NA
5) Kuhl 1990	Trauma patients requiring PN N = 20	C.Random: not sure ITT: yes Blinding: no (8)	46 % BCAA vs. 21 % BCAA (standard)	BCAA 1/10 (10)	Standard 2/10 (20)	BCAA 9/10 (90)	Standard 9/10 (90)

Table 1 (continued). Randomized studies evaluating BCAA (PN) in critically ill patients

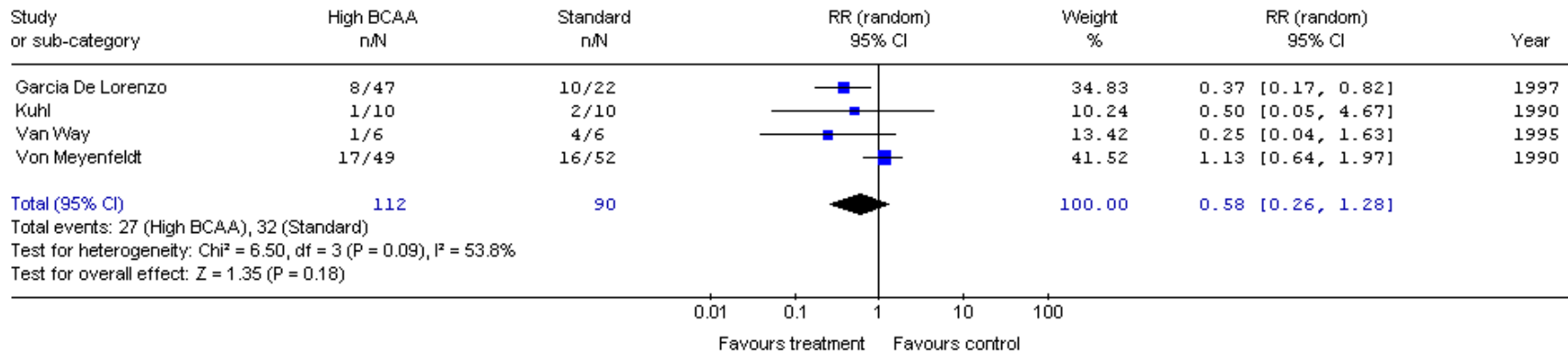
Study	LOS days		Ventilator days		Cost		Other	
	BCAA	Standard	BCAA	Standard	BCAA	Standard	BCAA	Standard
1) Ott 1988	BCAA NA	Standard NA	BCAA NA	Standard NA	BCAA NA	Standard NA	BCAA NA	Standard NA
2) Von Meyenfeldt 1990	BCAA NA	Standard NA	BCAA NA	Standard NA	BCAA NA	Standard NA	BCAA NA	Standard NA
3) Van Way 1995	BCAA NA	Standard NA	BCAA NA	Standard NA	BCAA NA	Standard NA	BCAA NA	Standard NA
4) Garcia De Lorenzo 1997	(A) ICU 18.5	(B) 14.4	(C) 17.8	NA	NA	NA	NA	NA
5) Kuhl 1990	BCAA NA	Standard NA	BCAA NA	Standard NA	BCAA NA	Standard NA	BCAA NA	Standard NA

C. Random: concealed randomization  
 ITT: intent to treat  
 BCAA: Branched chain amino acids  
 AA: amino acids

NA: not available  
 \*\* RR= relative risk, CI= Confidence intervals  
 ‡ number of patients with infections unless specified

Figure 1.

Review: Branched Chain Amino Acids  
 Comparison: 01 High BCAA vs. Standard  
 Outcome: 01 Mortality



**TOPIC: 9.1 Composition of PN: Branched Chain Amino Acids**

**Article inclusion log**

**Criteria for study selection**

<b>Type of study: RCT or Meta-analysis</b>
<b>Population: critically ill, ventilated patients (no elective surgery patients)</b>
<b>Intervention: PN</b>
<b>Outcomes: mortality, LOS, QOL, functional recovery, complications, cost. Exclude studies with only biochemical, metabolic or nutritional outcomes.</b>

	<b>Author</b>	<b>Journal</b>	<b>I</b>	<b>E</b>	<b>Why rejected</b>
1	Rossi-Fanelli	Digestive Diseases & Sciences 1982		√	Not ICU pts
2	Cerra	CCMedicine 1983		√	No clinical outcomes
3	Wahren	Hepatology 1983		√	Not ICU pts
4	Cerra	JPEN 1985		√	Not ICU pts
5	Iapichino	Clinical Nutrition '85		√	No clinical outcomes
6	Van Way	Am Surgeon 1985	√		
7	Bower	Annals Surgery 1986		√	No clinical outcomes
8	Vander Woude	CCMedicine 1986		√	Crossover RCT
9	Chiarla	J Trauma 1988		√	No clinical outcomes
10	Ott	Drug Intell Clin Pharm 1988	√		
11	Naylor	Gastroenterology 1989		√	Not ICU patients
12	Kuhl	Surgery 1990	√		
13	Von Meyenfeldt	Br J Surgery 1990	√		
14	Jiminez	JPEN 1991		√	Pseudorandomized
15	Vente	World J Surg 1991	√		No clinical outcomes
16	Garcia De Lorenzo	CCMedicine 1997	√		

I = included, E = excluded

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